IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent application of:
Reguri Buchi REDDY et al.

Application No.: 10/761,803

Filed: January 21, 2004

For: PROCESS FOR THE PREPARATION OF RISPERIDONE

Date: February 23, 2005
Atty. Docket No.: BULK 3.0-035
(Former Docket No. U 015001-7)

Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

TRANSMITTAL LETTER

Enclosed is a certified copy of the priority document for the subject application, India Patent Application 62/MAS 2003 filed January 21, 2003. This submission should complete the applicants' priority claim.

The owners of this application wish to formally appoint attorneys for further proceedings, and therefore are enclosing Forms PTO/SB/80 and PTO/SB/96.

Please change the address for correspondence to that of **Customer No. 45776**, and enter the new attorneys' **Docket No. BULK 3.0-022**.

Respectfully submitted,

Robert A. Franks
Attorney for Applicants
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THE PATENTS ACT, 1970

It is hereby certified that annexed hereto is a true copy of Application, Complete Specification, Abstract & Drawings of the extract of Patent Application No.62/MAS/2003, dated 21/01/2003 by M/s. Dr. Reddy's Laboratories Limited, having its registered office at 7-1-27, Ameerpet, Hyderabad 500 016, Andhra Pradesh, India.

.....

CERTIFIED COPY OF
PRIORITY DOCUMENT

.....In witness thereof

I have hereunto set my hand

Dated this the 26th day of July 2004

M.S. Venkataraman

(M.S. VENKATARAMAN)
Assistant Controller of Patents & Designs

PATENT OFFICE BRANCH
GOVERNMENT OF INDIA
Guindy Complex, 6th Floor, Annex.II
No.[illegible]3, A[illegible] Salai, Teynampet, Chennai – 600 018

FORM 1

THE PATENTS ACT, 1970
(39 of 1970)
APPLICATION FOR GRANT OF A PATENT
(Section 5(2), 7, 54 and 135 and Rule 33A)

1. We, Dr. Reddy's Laboratories Limited, an Indian company having its registered office at 7-1-27, Ameerpet, Hyderabad, Andhra Pradesh, INDIA, 500 016
2. hereby declare -
   (a) that we are in possession of an invention titled " **process for the preparation of crystalline form of 3-[2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a] pyrimidin-4-one (Risperidone)** "
   (b) that the Complete specification relating to this invention is filed with this application.
   (c) that there is no lawful ground of objection to the grant of a patent to us.
3. further declare that the inventor(s) for the said invention are **Reguri Buchi Reddy, Chakka Ramesh, Tamma Ranga Reddy and Kandirelli Venkata Kiran Kumar.** All citizens & residents of India belonging to **Dr. Reddy's Laboratories Limited, 7-1-27, Ameerpet, Hyderabad – 500 016, Andhra Pradesh.**
4. We claim the priority from the application(s) filed in convention countries, particulars of which are as follows.
5. We state that the said invention is an improvement in or modification of the invention, the particulars of which are as follows and of which We are the applicant
6. We state that the application is divided out of my/our application, the particulars of which are given below and pray that this application deemed to have been filed on _____ under section 16 of the Act.
7. That We are the assignee or legal representative of the true and first inventors.
8. That our address for service in India is as follows:

Dr. Reguri Buchi Reddy
Director R&D
Dr. Reddy's Laboratories Limited
7-1-27, Ameerpet
Hyderabad, A.P., 500 016
Phone: 040- 23095578
Fax: 040-3095438

9. Following declaration was given by the inventor(s) in the convention country: We, the true and first inventors for this invention in the convention country declare that the applicant(s) herein are our assignee or legal representative

(Signed) _____

Buchi Reddy Reguri,
404, Balaji Residency,
88/A, MIGH,
Vengal Rao Nagar,
Hyderabad-500 038.

(Signed) _____

Ramesh Chakka,
Plot No. 11,
Uma Nagar,
New Bowenpally,
Secunderabad-500 011.

(Signed) _____

Tamma Ranga Reddy,
Plot No.146,
Vasanth Nagar,
Kukat pally,
Hyderabad- 500 072.

(Signed) _____

Kandirelli Venkata Kiran Kumar,
H.No.24, SBI Colony,
Near: J.K.C. College Road,
Guntur-522 006.

10. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application.

11. Following are the attachments with the application
(a) Complete specification (---12--- pages, in triplicate)
(b) Drawings (-~~02~~- pages, in triplicate)
(c) Priority documents(s)
(d) Statement and Undertaking on Form-3.

(e) Power of authority
(f) Abstract of the invention (---01-- page, in triplicate)
(g) Fee Rs. 5000.00 (five thousand rupees only) in Cash/cheque/bank draft bearing No. 827600 dated January 16, 2003 drawn on HDFC Bank, Lakdikapul, Hyderabad-500 004.

We request that a patent may be granted to me/us for the said invention.

Dated this 17 th day of January 2003.

(Signed) _____

Dr. Reguri Buchi Reddy
Director (R&D)
Dr. Reddy's Laboratories Limited.

To,
The Controller of Patents
The Patents Office Branch, Chennai.

FORM 2

THE PATENTS ACT, 1970

COMPLETE SPECIFICATION

(SECTION 10)

Process for the preparation of crystalline form of 3-[2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (Risperidone)

Dr. Reddy's Laboratories ltd

An Indian Company having its registered office at

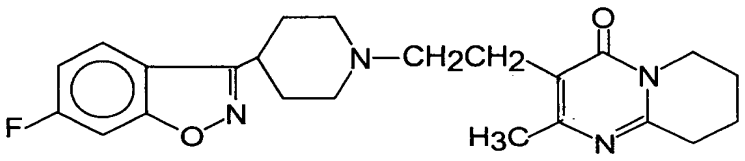
7-1-27, Ameerpet

Hyderabad – 500 016, A.P., India

The following specification particularly describes the nature of this invention and the manner in which it is to be performed:

FIELD OF INVENTION

The present invention relates to process for the preparation of crystalline form of 3-[2-[4-(6-Fluoro-1, 2-benzisoxazol-3-yl)-1-piperidinyl] ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido [1,2-a] pyrimidin-4-one. The product is also known as Risperidone in therapy and Risperidal as one of its familiar brand names. It may be represented by the following formula I.



Formula I

BACKGROUND OF THE INVENTION

European patent EP 196132 B1 discloses certain 1,2-benzisoxazol-3-yl derivatives having psychotic and anti-serotonin activity including 3-[2-[4-(6-Fluoro-1, 2-benzisoxazol-3-yl)-1-piperidinyl] ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido [1,2-a] pyrimidin-4-one (Risperidone), which is a mixed 5-HT_{2A}/D_2-receptor antagonist and is an example of typical neuroleptic drug. The process for the preparation of Risperidone comprises condensation of two advanced intermediates i.e., 3-(2-chloroethyl)-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidine-4-one mono hydrochloride and 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole in a solvent using a base.

The latest trend that has, of late, crept into the pharmaceutical industry is the studies on polymorphism in drugs and the difference in the activity of different polymorphic forms of a given drug. By the polymorphism we mean different physical forms, crystal forms, crystalline/liquid crystalline/non crystalline (amorphous) forms. This has especially become very interesting after

observing that many antibiotics, antibacterials, tranquillisers etc. exhibit polymorphism and some/one of the polymorphic forms of a given drug exhibit superior bioavailability and consequently show much higher activity compared to other polymorphs.

The Summary Basis Of Approval (SBOA) submitted to the FDA by the inventors of Risperidone, disclose the existence of two polymorphic forms, polymorph 1 and polymorph 2 wherein polymorph 1 is stated as a more thermodynamically stable form, which is obtained by recrystallisation in Ethanol. However no substantial information is disclosed about polymorph 2 in prior art references.

The process disclosed in **EP 196132** for preparation of pure Risperidone (Example 5), comprises recrystallisation of crude Risperidone in a mixture of dimethyl formamide and isopropyl alcohol to afford pure Risperidone.

US application 2002/0115673 and 2002/0115672 also discloses the process for the preparation of Risperidone including the process for the preparation of polymorphs Form-A, Form-B and Form-E. The process for the preparation of Risperidone comprises similar condensation as mentioned above but in their base forms i.e., 3-(2-chloroethyl)-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidine-4-one and 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole using a solvent and a base.

X-ray powder diffractogram for EPCRS (European current reference standard) of Risperidone and X-ray powder diffractogram of the present invention are found to be similar indicating that the present invention is directed to prepare the EPCRS form of Risperidone.

The X-ray powder diffraction pattern of EPCRS of Risperidone is captured in the following table (table-1).

Table –1:

2-Theta	Intensity
7.137	2.5
10.751	4.4
11.544	8.1
14.343	37.5
14.964	13.3
15.546	4
16.510	9.3
18.652	12.6
18.992	22
19.923	17.1
21.386	100
22.236	4.1
22.541	11.1
23.300	25.1
23.620	6.7
24.556	2.1
25.403	3.8
27.619	3.9
28.663	3.7
29.077	14.7
32.574	2.3
33.260	3.5
38.642	2.1

The main objective of the present invention is to prepare the crystalline EPCRS form of 3-[2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (Risperidone), herein after termed as EPCRS for convenience.

SUMMARY OF THE INVENTION

The present invention is directed to provide a process for the preparation of EPCRS form of Risperidone. The present invention also embodies a process for the preparation of EPCRS crystalline form of Risperidone which comprises, heating the Risperidone in an organic solvent(s) followed by subsequent cooling and isolation to get desired polymorph of Risperidone.

BRIEF DESCRIPTION OF THE ACCOMPANYING DRAWINGS

Fig. 1 is X-ray powder diffractogram of EPCRS of Risperidone.

Fig. 2 is X-ray powder diffractogram of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

According to one aspect, the present invention provides a simple process for the preparation crystalline EPCRS form of Risperidone, which can be identified by X-ray powder diffraction as shown in Table – 2.

Table – 2

2-Theta	Intensity
7.144	3.3
10.787	4.2
11.581	13.5
14.354	75.3
14.961	18.8
15.621	6.8
16.571	11.5
18.625	22
19.067	28.5
19.929	24.6
21.430	100
22.319	9.2
22.613	13.2
23.313	29.5
23.621	8.3
24.495	2.6
25.428	5.5
27.672	5.8
28.534	8.2
29.156	15.7
32.570	3.1
33.147	2.5
38.718	1.6

The significant d values obtained are 7.144 ± 0.2 , 10.787± 0.2 , 11.581 ± 0.2 , 14.354 ± 0.2, 14.961 ± 0.2, 15.621± 0.2 , 16.571± 0.2, 18.625 ± 0.2, 19.067 ± 0.2, 19.929 ± 0.2, 21.430 ± 0.2, 22.319 ± 0.2, 22.613 ± 0.2, 23.313 ± 0.2, 23.621 ± 0.2, 24.495 ± 0.2, 25.428 ± 0.2, 27.672 ± 0.2, 28.534 ± 0.2 , 29.156 ± 0.2, 32.570 ± 0.2, 33.147 ± 0.2 and 38.718 ± 0.2.

The present invention also provides a simple process for the preparation of EPCRS form of Risperidone.

The crystalline EPCRS form of Risperidone of the present invention is prepared by a process, which comprises:

a) dissolving the Risperidone in an organic solvent(s) such as methyl propyl ketone, anisole, dioxane, methyl cellosolve, xylene, 1- pentanol, mixture of alcohols such as methanol or ethanol with solvents as acetone, methyl isobutyl ketone, methyl cellosolve, heptane, di-isopropyl ether, cyclohexane, isooctane, anisole, mixture of toluene with solvents such as acetone, iso octane, heptane, diisopropyl ether, mixture of xylene with solvents such as n-hexane, heptane, isooctane, t-butyl ether, mixture of methyl isobutyl ketone and methyl cellosolve, mixture of dichloromethane and iso octane, Mixture of methanol and water, Aqueous ethanol, mixture of chloroform and cyclohexane etc or a combination of above described solvents at hot condition or at reflux

b) optionally treating the dissolved solution with carbon

c) filtering the reaction solution to get particle free solution

d) cooling the reaction solution to get precipation / optionally adding the anti solvents such as n-hexane, n-heptane, isooctane, cyclohexane etc. for the separation of Risperidone from reaction solution.

e) isolating the desired EPCRS form of Risperidone by conventional methods.

The present invention hence is directed to the preparation of crystalline EPCRS form of Risperidone and also provides a simple and commercially viable process for its preparation.

The following examples illustrate the invention but do not limit it in any way.

Risperidone can be prepared by the disclosed methods in EP 196132, US 2002/0115673A1 or US 2002/0115672A1.

Examples

Example 1:

Toluene (90.0 ml) was added to the Risperidone (10.0 g.) and then heated to reflux and observed dissolution. Treated the hot reaction solution with carbon (1.0 g) and filtered. The reaction solution was then added to iso octane (80.0 ml) consisting in another flask slowly at 25 – 35^{O} C. The reaction mass was stirred for 1 – 2hours at 25 – 35^{O} C and filtered. Washing the precipitate with iso-octane (10.0 ml) followed by drying produced the EPCRS of Risperidone (Yield 8.1g, 81%).

Example 2:

Methyl isobutyl ketone (15.0 ml) and methyl cellosolve (15.0 ml) was added to the Risperidone (5.0 g.) and then heated to reflux and observed dissolution. Treated the hot reaction solution with carbon (0.5 g) and filtered. The reaction solution was then cooled to 0 – 5^{O} C and maintained at the same temperature for 1 – 2 hours. Filtered the separated solid and washed with methyl isobutyl ketone (5.0 ml). Drying the resulted product produced the EPCRS of Risperidone (Yield 3.1g, 62%).

Example 3:

Methyl propyl ketone (30.0 ml) was added to the Risperidone (5.0 g.) and then heated to reflux and observed dissolution. The reaction solution maintained at reflux for 5 – 20 minutes and filtered. The reaction mass was cooled to 25 – 35^{O} C and stirred at the same temperature for 1- 2 hours and

filtered. Washing the precipitate with methyl propyl ketone (5.0 ml) followed by drying produced the EPCRS of Risperidone (Yield 3.6 g, 72%).

Example-4 :

Xylene (25.0 ml) was added to the Risperidone (5.0 g.) and then heated to reflux and observed dissolution. The reaction solution maintained at reflux for 5 – 15 minutes and filtered. The reaction mass was cooled to 25 – 35^{O} C and stirred at the same temperature for 1- 2 hours and filtered. Washing the precipitate with xylene (5.0 ml) followed by drying produced the EPCRS of Risperidone (Yield 3.4 g, 68%).

Example-5 :

1-Pentanol (25.0 ml) was added to the Risperidone (5.0 g.) and then heated to reflux and observed dissolution. The reaction solution maintained at reflux for 15 – 30minutes and filtered. The reaction mass was cooled to 25 – 35^{O} C and stirred at the same temperature for 1- 2 hours and filtered. Washing the precipitate with 1-pentanol (5.0 ml) followed by drying produced the EPCRS of Risperidone (Yield 3.4 g, 68%).

Example-6 :

20% Aqueous ethanol (60.0 ml) was added to the Risperidone (10.0 g.) and then heated to reflux and observed dissolution. Treated the hot reaction solution with carbon (1.0 g) and filtered. The reaction solution was then cooled to 0 – 5^{O} C and maintained at the same temperature for 30 – 60 minutes. Filtered the separated solid and washed with 20% aqueous ethanol (5.0 ml). Drying the resulted product produced the EPCRS of Risperidone (Yield 5.3 g, 53%).

Example 7:

Anisole (10.0 ml) and ethanol (10.0 ml) was added to the Risperidone (10.0 g.) and then heated to reflux and observed dissolution. Treated the hot reaction solution with carbon (1.0 g) and filtered. The reaction solution was then cooled to 0 – 5^{O} C and maintained at the same temperature for 30-60 minutes. Filtered the separated solid and washed with a mixture of anisole (0.25ml) and

ethanol (0.25 ml). Drying the resulted product produced the EPCRS of Risperidone (Yield 4.8g, 48%).

Example 8:

Water (50.0 ml) was added to the Risperidone (50.0 g.) and then added acetic acid (7.8 ml) and stirred for 5 – 10 minutes. Filtered the un-dissolved portion, washed with water (25.0 ml) and to the combined filtrate methanol (200.0 ml) was added. Adjust the pH of the reaction mass to 8 – 9 with methanolic sodium hydroxide (6 g sodium hydroxide in 60 ml methanol). Stirred the suspension for about 30 – 60 minutes at 20 –35^{O} C and then heated the contents to reflux and observed dissolution. Treated the hot reaction solution with carbon (5.0 g), filtered and washed the carbon bed with methanol (10.0 ml). Transferred the filtrate into an another flask, stirred at 20 – 30^{O}C for 30 – 60 minutes, filtered and washed with water (50.0 ml) The solid was taken in water (200 ml) and stirred at 25 – 35^{O} C for 30 – 60 minutes. Filtration followed by washing with water (50 ml), methanol (50.0 ml) and subsequent drying produced EPCRS of Risperidone

(Yield 32.6 g, 65.2 %).

The crystalline EPCRS polymorph of Risperidone obtained from above examples has similar XRD pattern in accordance with Figure (2).

DETAILED DESCRIPTION OF THE ACCOMPANYING DRAWINGS

Fig. 1 is characteristic X-ray powder diffraction pattern of EPCRS of Risperidone.

Vertical axis: Intensity (CPS); Horizontal axis: 2 Theta (degrees).

The X-Ray diffraction pattern of EPCRS of Risperidone was measured on a Rigaku D/Max 2200 Powder Diffractometer with Cu Radiation source.

The significant two theta values obtained are 7.144, 10.787, 11.581, 14.354, 14.961, 15.621, 16.571, 18.625, 19.067, 19.929, 21.340, 22.319, 22.613, 23.313, 23.621, 24.495, 25.428, 27.672, 28.534, 29.156, 32.570, 33.147 and 38.718.

Fig. 2 is characteristic X-ray powder diffraction pattern of Polymorphic form of Risperidone obtained from the above examples.

Vertical axis: Intensity (CPS); Horizontal axis: 2 Theta (degrees).

The X-Ray diffraction pattern of the present invention process of Risperidone was measured on a Rigaku D/Max 2200 Powder Diffractometer with Cu Radiation source.

The significant d values obtained are 7.144 $\pm$ 0.2 , 10.787$\pm$ 0.2 , 11.581 $\pm$ 0.2 , 14.354 $\pm$ 0.2, 14.961 $\pm$ 0.2, 15.621$\pm$ 0.2 , 16.571$\pm$ 0.2, 18.625 $\pm$ 0.2, 19.067 $\pm$ 0.2, 19.929 $\pm$ 0.2, 21.430 $\pm$ 0.2, 22.319 $\pm$ 0.2, 22.613 $\pm$ 0.2, 23.313 $\pm$ 0.2, 23.621 $\pm$ 0.2, 24.495 $\pm$ 0.2, 25.428 $\pm$ 0.2, 27.672 $\pm$ 0.2, 28.534 $\pm$ 0.2 , 29.156 $\pm$ 0.2, 32.570 $\pm$ 0.2, 33.147 $\pm$ 0.2 and 38.718 $\pm$ 0.2.

We claim :

1. A novel process for the preparation of EPCRS form of 3-[2-[4-(6-Fluoro-1, 2-benzisoxazol-3-yl)-1-piperidinyl] ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido [1,2-a] pyrimidin-4-one (Risperidone), which comprises:

a) dissolving the Risperidone in an organic solvent(s) such as methyl propyl ketone, anisole, dioxane, methyl cellosolve, xylene, 1- pentanol, mixture of alcohols such as methanol or ethanol with solvents as acetone, methyl isobutyl ketone, methyl cellosolve, heptane, di-isopropyl ether, cyclohexane, isooctane, anisole, mixture of toluene with solvents such as acetone, iso octane, heptane, diisopropyl ether, mixture of xylene with solvents such as n-hexane, heptane, isooctane, t-butyl ether, mixture of methyl isobutyl ketone and methyl cellosolve, mixture of dichloromethane and iso octane, Mixture of methanol and water, Aqueous ethanol, mixture of chloroform and cyclohexane etc or a combination of above described solvents at hot condition or at reflux

b) optionally treating the dissolved solution with carbon

c) filtering the reaction solution to get particle free solution

d) cooling the reaction solution to get precipitation / optionally adding the anti solvents such as n-hexane, n-heptane, isooctane, cyclohexane etc. for the separation of Risperidone from reaction solution.

e) isolating the desired EPCRS form of Risperidone by conventional methods.

2. The process as claimed in claim 1 of step (a), dissolving the Risperidone in an organic solvent selected from methyl propyl ketone, anisole, dioxane, methyl cellosolve, methyl cellosolve, xylene and 1- pentanol .

3. The process as claimed in claim 1 of step (a), dissolving the Risperidone in a solvent mixture of alcohols such as methanol or ethanol with solvents like acetone, methyl isobutyl ketone, methyl cellosolve, n-heptane, di-isopropyl ether, cyclohexane, isooctane and anisole.

4. The process as claimed in claim 1 of step (a), dissolving the Risperidone in a solvent mixture of toluene or Xylene with solvents such as acetone, heptane, diisopropyl ether, n-hexane, , isooctane and t-butyl ether.

5. The process as claimed in claim 1 of step (a), dissolving the Risperidone in a solvent mixture of methyl isobutyl ketone and methyl cellosolve

6. The process as claimed in claim 1 of step (a), dissolving the Risperidone in a solvent mixture of dichloromethane and isooctane

7. The process as claimed in claim 1 of step (a), dissolving the Risperidone in a solvent mixture of methanol and water.

8. The process as claimed in claim 1 of step (a), dissolving the Risperidone in Aqueous ethanol.

9. The process as claimed in claim 1 of step (a), dissolving the Risperidone in a mixture of chloroform and cyclohexane.

10. The process as claimed in claim 1 of step (a), dissolving the Risperidone in an Aqueous ethanol ranging 1% to 30%(water content in ethanol).

11. The process as claimed in claim 1 of step (a), dissolving the Risperidone in a solvent or solvents at hot condition ranging from 40°C to reflux temperature.

12. The process as claimed in claim 1 of step (a), where in dissolving the Risperidone in a solvent or solvents mixture selected from any of the mentioned solvents in step(a) of claim 1.

13. The crystalline EPCRS form of Risperidone obtained in the process of claim 1 has X-ray powder diffraction pattern with peaks at 7.144 ± 0.2 , 10.787± 0.2 , 11.581 ± 0.2 , 14.354 ± 0.2, 14.961 ± 0.2, 15.621± 0.2 , 16.571± 0.2, 18.625 ± 0.2, 19.067 ± 0.2, 19.929 ± 0.2, 21.430 ± 0.2, 22.319 ± 0.2, 22.613 ± 0.2, 23.313 ± 0.2, 23.621 ± 0.2, 24.495 ± 0.2, 25.428 ± 0.2, 27.672 ± 0.2, 28.534 ± 0.2 , 29.156 ± 0.2, 32.570 ± 0.2, 33.147 ± 0.2 and 38.718 ± 0.2. degrees two theta.

14. The process for the preparation of crystalline EPCRS form of Risperidone as herein described with particular reference to examples.

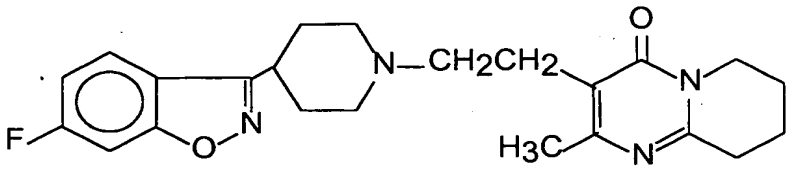
Dated 16th day of January, 2003

Signed _____
Dr. Reguri Buchi Reddy
Director (R&D),
Dr. Reddy's Laboratories Limited.

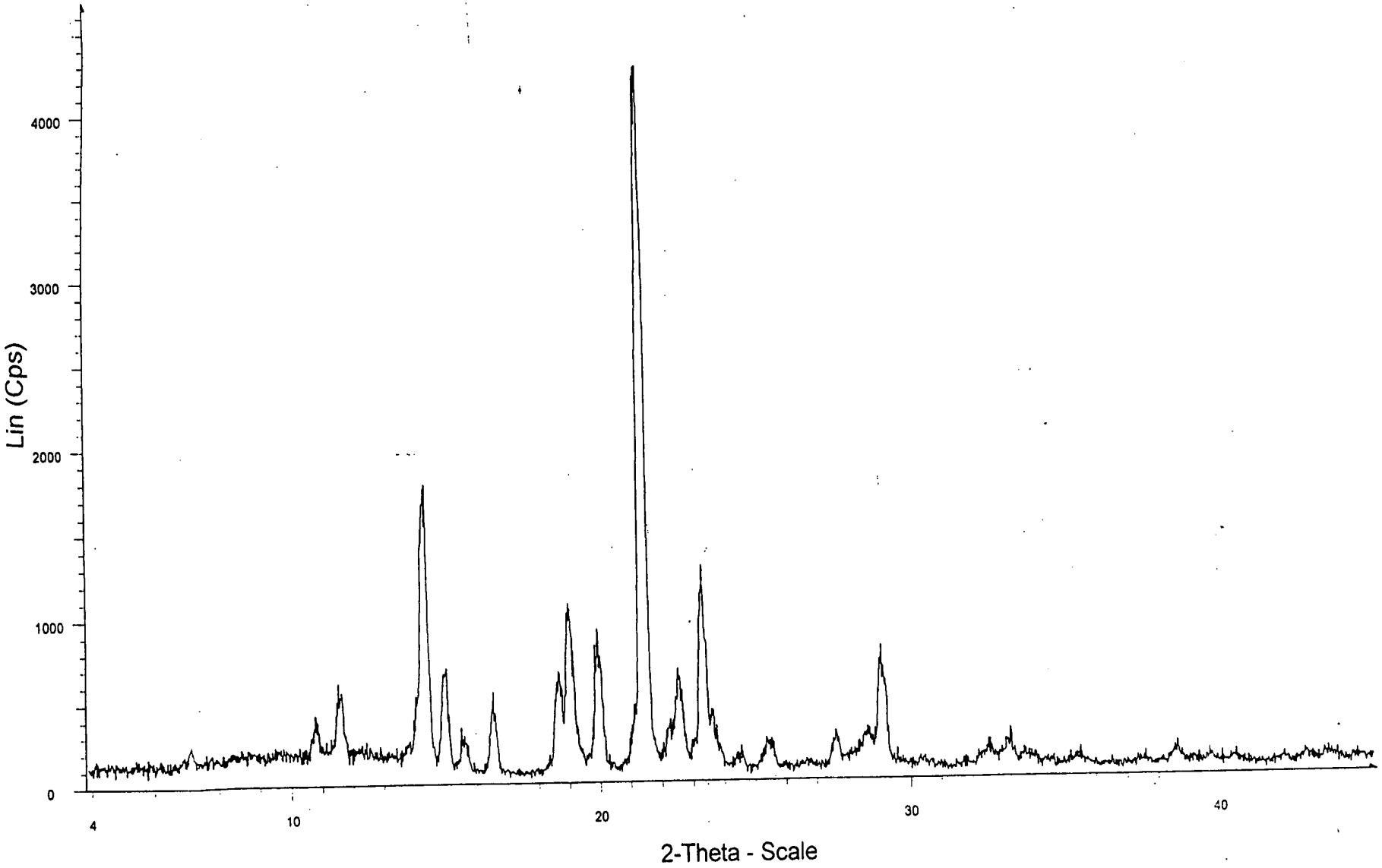
ABSTRACT

Title of the invention: "process for the preparation of crystalline form of 3-[2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a] pyrimidin-4-one (Risperidone)"

The Present invention is directed to provide a process for the preparation of EPCRS form of Risperidone. The present invention also embodies a process for the preparation of EPCRS crystalline form of Risperidone which comprises, heating the Risperidone in an organic solvent(s) followed by subsequent cooling and isolation to get desired polymorph of Risperidone (Formula I).

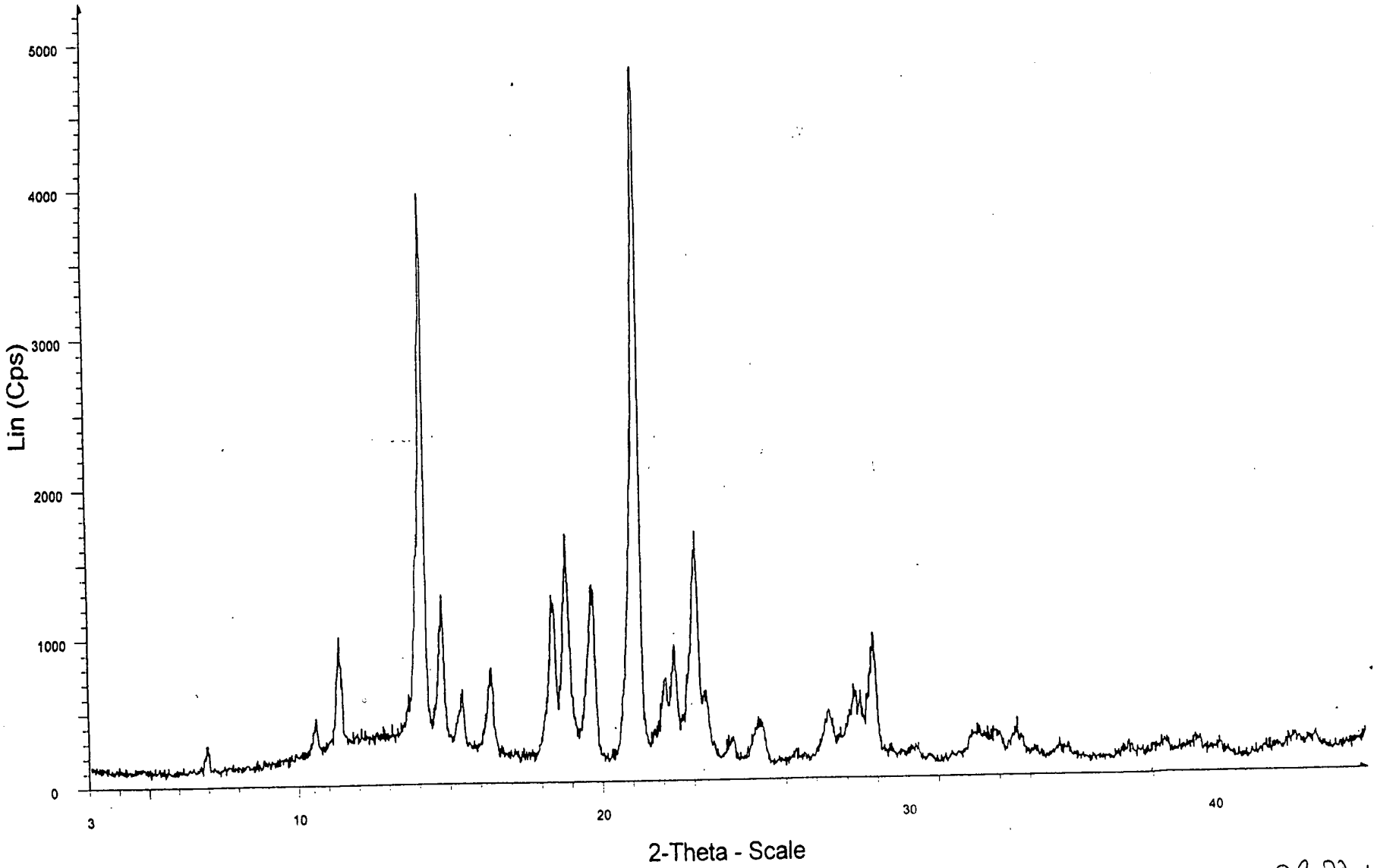


Formula I



Dr. Reguri Buchi Reddy

DR. Reddy's Laboratories Limited.



Dr. Reguri Buchi Reddy